| Publications | Grade | Quality | Comments |
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| Mouncey PR, et al. Trial of early, goal-directed resuscitation for septic shock. NEJM 2015; 372:1301-11. | A | Outstanding | • Non-blinded intervention<br>• Mortality lower than expected<br>• Patients got lower volumes of IVFs and more vasopressors compared with Rivers et al. |
| ARISE Investigators. Goal-directed resuscitation for patients with early septic shock. NEJM 2014; 371:1496-506. | A | Outstanding | • Not blinded<br>• Mortality rate lower than original EGDT trial |
| ProCESS Investigators. A randomized trial of protocol-based care for early septic shock. NEJM 2014; 370: 1683-93. | A | Outstanding | • Baseline mortality differences b/w Rivers et al.<br>• Mean ScvO2 different between Rivers et al. |
| Andrews B, Muchemwa L, Kelly P, et al. Simplified severe sepsis protocol: a randomized controlled trial of modified early goal-directed therapy in Zambia. Crit Care Med 2014; 42:2315-24. | A | Adequate | • Single center in Zambia<br>• Non-blinded<br>• 81% HIV positive pts; Mean CD4 49<br>• Stopped early due to high mortality among patients with hypoxemic respiratory failure in intervention arm<br>• Protocol consisted of IVFs, dopamine, blood transfusions<br>• Used JVP to assess volume due to limited resource setting<br>• No change in mortality |
| Coen D, Cortellano F, Pasini S, et al. Towards a less invasive approach to the early goal-directed treatment of septic shock in the ED. Am J Emerg Med 2014; 32:563-8. | C | Poor | • Single-center<br>• 51 patients<br>• No comparison group<br>• More cancer and immunosuppressed patients than Rivers trial |

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| Cannon CM, Holthaus CV, Zubrow MT, et al. The GENESIS project (GENeralized Early Sepsis Intervention Strategies): a multicenter quality improvement collaborative. J Intensive Care Med 2013; 28:355-68. | C | Good | • A CQI initiative<br>• Before-and-after study with historical controls<br>• Community and academic hospitals<br>• Included patients from ED, general ward, and ICU<br>• Absolute and relative mortality decrease between groups<br>• CVP and ScvO2 not significant predictor of mortality |
| Jones AE, Troyer JL, Kline JA. Cost-effectiveness of an emergency department-based early sepsis resuscitation protocol. Crit Care Med 2011; 39:1306-12. | C | Adequate | • Before-and-after study<br>• Single center<br>• Cost effectiveness of implementing EGDT protocol<br>• EGDT protocol did not included dedicated team<br>• EGDT increased hospital cost by approx.. $7000;<br>• In-hospital mortality lower<br>• $5400 QALY gained |
| Suarez D, Ferrer R, Artigas A, et al. Cost-effectiveness of the Surviving Sepsis Campaign protocol for severe sepsis: a prospective nation-wide study in Spain. Intensive Care Med 2011; 37:444-52. | C | Adequate | • Prospective, before-and-after study<br>• 59 ICUs in Spain<br>• In-hospital mortality lower (44% vs. 39.7%)<br>• SSC protocol had higher costs and longer LOS<br>• Mean life years gained higher in the SSC protocol cohort<br>• Divided into resuscitation bundles and management bundles<br>• Treatment varied within cohorts; management did not always comply with bundles |

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| Castellanos-Ortega A, Suberviola B, Garcia-Astudillo LA, et al. Impact of the Surviving Sepsis Campaign protocols on hospital length of stay and mortality in septic shock patients: results of a three-year follow-up quasi-experimental study. Crit Care Med 2010; 38:1036-43. | C | Adequate | • Prospective, before-and-after study<br>• Single-center med-surg ICU in Spain<br>• 6-hr resuscitation bundle delivered in ICU, not ED<br>• 384 in intervention group; 43 completed all 7 tasks in resuscitation bundle<br>• ScvO2 of > 70% was only intervention of statistical significance<br>• Mortality lower 57.3% vs. 37.5% in intervention group |